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METAL SALT CATALYZED CARBENOIDS—XIV[1]

THE MECHANISMS OF CARBENE DIMER FORMATION FROM DIAZOACETIC ESTER AND DIMETHYL DIAZOMALONATE IN THE PRESENCE OF SOME SOLUBLE COPPER CATALYSTS

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Abstract—An examination of partial rate data for the decomposition of diazo acetic ester and dimethyl diazomalonate, in the presence of soluble copper salts and cyclohexene, revealed the existence of two paths to carbene dimer formation, one with a unimolecular dependence upon catalyst, the other with a bimolecular dependence. Assuming carbenoid formation, this is taken as indicative of dimer formation occurring by carbenoid + diazo compound and carbenoid + carbenoid paths. Conformational analyses indicate a preference for diethyl maleate formation by the carbenoid-diazo ester path for the case of diazoacetic ester and a preference for diethyl fumarate formation by the carbenoid + carbenoid path.

INTRODUCTION

The formation of carbenoid dimers[4] from carbenes[5] and copper catalyzed carbenoid processes[6] is well known and has found some synthetic utility.[7] The reaction is most frequently encountered as a side process and with equal frequency is not treated as anything other than an annoying side reaction suitable for omission in subsequent abstracting.[8] The reaction is thought to bear a resemblance to olefin disproportionation reactions.[9] Although there are several examples of a carbene dimerizing,[5] it seems most probable that the processes are more common with catalyzed reactions. This is not particularly suprising since carbenes are generally high energy species and direct dimerization would normally be expected to occur by low probability three body collisions.

The present work was initiated for two basic reasons, (a) partial rate data indicated that the decomposition of dimethyl diazomalonate was of mixed order in catalyst, and (b) the literature reported obviously contradictory results on dimer formation from diazoacetic ester. Thus, at least one worker has found exclusive diethyl maleate formation while others have found various mixtures of fumarates and maleates. The authors are extremely dubious of all claims that the trimer (cyclopropane) from diazoacetic ester is generated directly[10] if at all and suspect more rigorous analyses of existing claims will indicate the products are pyrazolines or pyrazoline derived.[11] Numerous unsuccessful attempts were made to form the "trimer cyclopropanes" from diazoacetic ester, dimethyl diazomalonate and di-t-butyl diazomalonate.

It was initially hoped that it would be possible to distinguish between the **MμS** and **SMμ** mechanisms[12] for dimer formation. Although both observed processes clearly are of a **MT-2** type,[12] the distinction between initial attack on carbon or copper was not possible because one can not presently establish whether *cis* or *trans* eliminations are occurring in the step leading to products (*vide infra*).

RESULTS AND DISCUSSION

In our initial studies[13] with diazomalonates we employed alkylphosphite complexes of copper(I) salts. The fact that the formal catalyst is rapidly destroyed by diazo compound makes it extremely questionable to draw

Table 1.

mmole of cat. and N	Products and Yields 8		9		8/9	10		11		10/11
	Absolute	Relative	Absolute	Relative	Ratio	Absolute	Relative	Absolute	Relative	Ratio
N=1										
0.14	7 80	1	0.65	0.083	12.0	0.088	0.011	0.123	0.015	0.715
5.0	2.91	1	1.16	0.390	2.51	0.218	0.075	0.710	0 244	0.307
N=2										
0.14	7.37	1	0.684	0.087	11.5	0.100	0.012	0.150	0.019	0.667
5.0	0.965	1	0.946	0.960	1.02	0.077	0.079	0.254	0.263	0.304
N=3										
0.14	6.05	1	0.533	0.066	15.1	0.067	0.008	0.111	0.013	0.608
5 0	0.333	1	0.832	2.50	0.400	none		none		

Absolute yields relative to internal standard. Catalyst= $[(CH_3O)_3P]_NCuI$
Real yield is approximately 10x Absolute.

extensive mechanistic conclusions.[14] When diazoacetic ester was decomposed at two different catalyst concentrations with three different catalysts of this type there was a clear difference in stereoselectivity (Table 1). Since some workers apparently believe that copper(II) catalyzes the dimerization reactions and copper(I) the cyclopropanation reactions,[15] and because the formal catalysts were clearly not surviving the reaction, we examined the same reaction with *bis*-acetylacetonato copper(II) as catalyst. The results (Table 2) were similar to those obtained with the phosphite based catalysts. The general trend is towards favoring the *cis* isomer at low catalyst concentrations. The "zero catalyst concentration" point in Table 2 is of interest not because it indicates the presence of a thermal path to dimer (we found none) but rather that the use of glassware previously exposed to copper salts leads to catalytically active apparatus. Thus, the history of the apparatus as well as more normal variables such as temperature, concentration and solvent plays an important role in generating useful and comparable data.

Table 2.

Catalyst Concentration mg/50ml	Trans (11)/Cis (10)
0	0.53
1	0.69
4	0.69
16	0.89
32	1.03
64	1.39
256	2.18

Catalyst · Cu(II)AcAc$_2$

The obvious interpretation of the data obtained is that two different reactions lead to the same products with one being more favorably disposed to formation of the *cis* isomer. In neither case would it appear likely that the reactions are stereospecific. The simplest rationale to account for this behavior is to have two processes one of which is unimolecular in catalyst and the other which is bimolecular (eqns 1–3).

Possible rate expressions

$$\text{Rate of } \alpha\,[\text{catalyst}][\text{diazo}]^2 + [\text{catalyst}]^2[\text{diazo}]^2 \tag{1}$$

or

$$[\text{carbenoid}][\text{diazo}] + [\text{carbenoid}][\text{diazo}][\text{catalyst}] \tag{2}$$

or

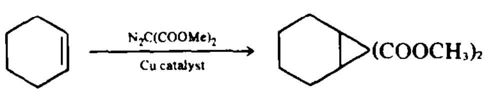
$$[\text{carbenoid}][\text{diazo}] + [\text{carbenoid}]^2 \tag{3}$$

This extrapolates smoothly to paths involving reaction of carbenoid + diazo compound and carbenoid + carbenoid. One might also write non-carbenoid paths involving complexed diazo compound and obtain similar type results. The existence of carbenoids is therefore not *conditio sine qua non* but is only employed for convenience and because on an intuitive basis we believe carbenoids are involved.

The change of molecularity in catalyst is also evident from the partial rate data obtained with dimethyl diazomalonate in olefinic solutions.[13] Thus, the fact that dimer formation becomes increasingly more favorable at high catalyst concentrations as it competes with cyclopropanation and allylic C–H insertion, is only consistent with the proposed mixed molecularity situation (see reference 16 for additional arguments) with increased catalyst concentration, the effective concentration of diazo-compound will decrease under the reaction conditions employed.[17]

In any event, the processes are clearly of a MT-2 type and analyses of the stereochemical preferences can be made employing this formalism.

The distinction between the **MμS** and **SMμ** processes coupled with four center versus two center approaches of reactants leads to the eleven basic mechanistic schemes (Schemes A–L). In each of these schemes we have represented the situation expected to be most favorable



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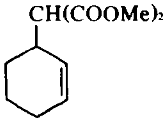

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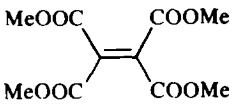

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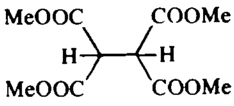

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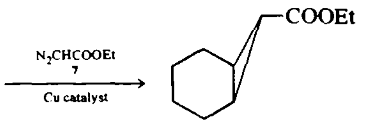

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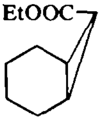

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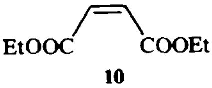

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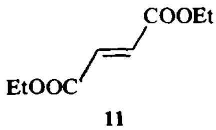

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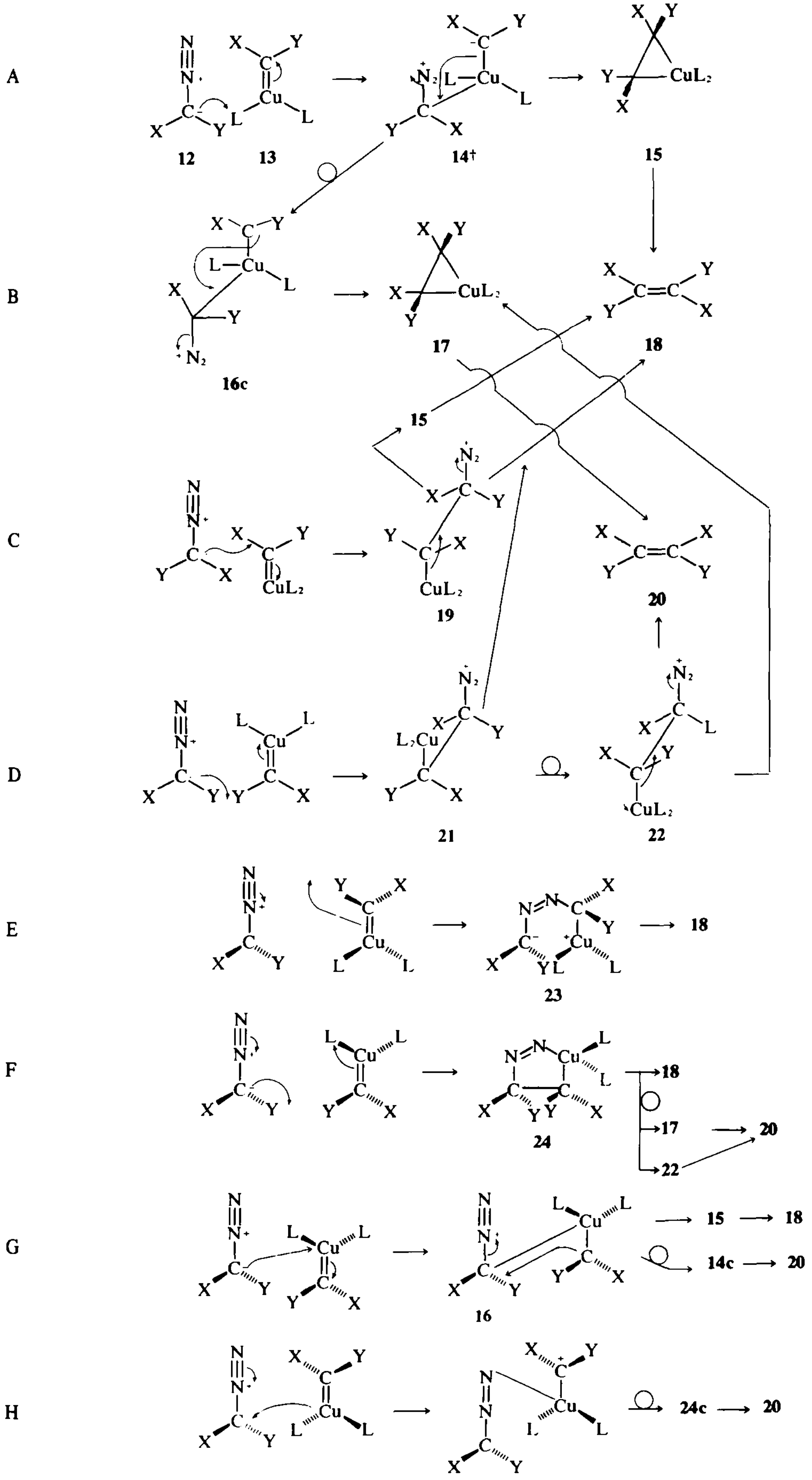
A
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14†
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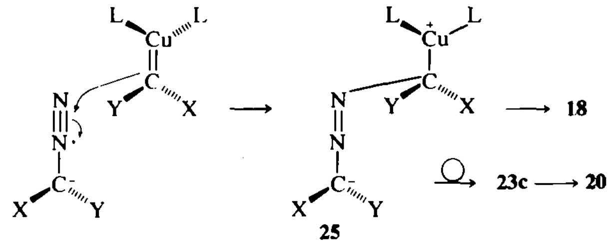

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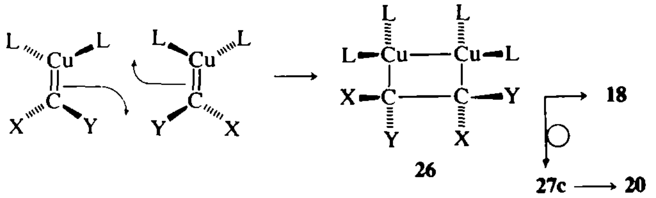

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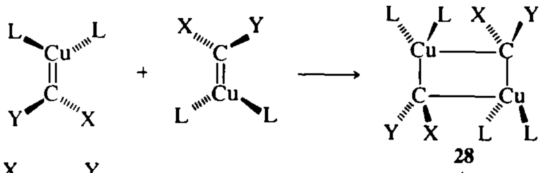

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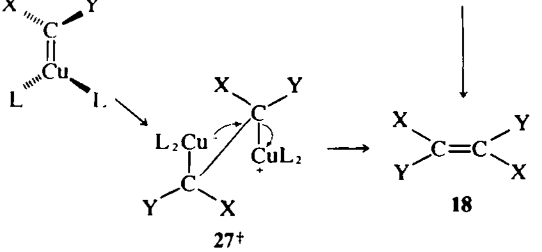

on the basis that like groups repell and bulky substituents will tend to be as far from each other as possible.

Although the number of possibilities is large it is possible to eliminate some on the basis of quite simple arguments. Thus any system which places a positive charge on copper is unlikely since the carbenoid reacts most readily when an associated ligand on carbon can bear a negative charge. The resulting formal valence of copper (+) in those cases would be three. Hence schemes **E** and **I**, represent improbable paths. Similarly path **H** places a positive charge on carbon and this seems highly unlikely since the groups **X** and sometimes **Y** in our investigations have been election withdrawing groups.

In the case of all 4 center combinations (**A**, **B**, **E**, **F**) *cis* eliminations of N_2 and/or CuL_2 favors the *trans* olefins contrary to the real situation. One would expect the intermediates **15** and **17** to lose CuL_2 in a *cis* fashion and thus we can eliminate path **A**.

Since the use of the bulky catalyst *bis* pivaloylmethanato copper(II) (Table 3) retards cyclopropanation which involves a copper-substrate interaction, but does not greatly hinder dimerization, it would seem unlikely that any tight 4 center mechanism is involved. Thus we might discard **A**, **D**, **E** and **F** and **B** which arose via **A**. Of the remaining two paths **C** and **G**, **G** proceeds via **15** to the *trans* olefin **18** and **C** furnishes **18** as well. This accounts for all paths, however **D** and **F** are especially attractive because the steric requirements of the N_2 group is very small, there need be little or no interaction between N and Cu, and in each case a *trans* elimination would be expected to occur from the intermediate **22** to furnish the *cis* olefin **20** or a *cis* elimination from the intermediate **17** which would also furnish **20**, we favor **D** over **F** on the basis that the carbenoid is most probably electron deficient and the carbon of the diazo compound is electron rich.

All of the above would be meaningless if we obtained the same predictions for the carbenoid + carbenoid reaction. However, Paths **J**, **K** and **L** predict a preference for *trans* olefin; the experimentally observed phenomenon. We do not like paths **J** and **K** because they involve forbidden 2 + 2 cycloaddition reactions.

For both processes, we prefer the mechanisms involving initial C–C bond formation, **D** and **L**. The major reason for this preference lies in the conformational analyses of possible penta-coordinated intermediate.[12] In each case the steric problems are minimized and this seems to be a reasonable requirement when it is remembered that in the absence of olefinic substrates, dimer formation becomes an excellent high yield reaction.

With the extremely bulky catalyst *bis*-

Table 3. Copper (II) catalyst vs products in the reaction of diazomalonate in cyclohexene

Catalyst Ligand	Product Yield and (relative to norcarane) (3)	(4)	(5)	(6)
Dipivaloylmethane	0.89 (1.00)	0.07 (0.09)	6.75 (7.52)	3.99 (4.43)
Acetylacetone	79.45 (1.00)	2.54 (0.03	8.07 (0.10)	0.93 (0.01)

pivaloylmethanato copper(II), the dimerization is still a very good reaction whereas cyclopropanation becomes relatively unimportant (Table 3). The reverse situation holds with the acetylacetonato complex. Since the only major difference between the two catalysts is steric bulk, it seems probable that the ease of access to the metal during the dimerization process is of minimal importance.

Summary. Dimer formation occurs via two paths, carbenoid + diazo compound and carbenoid + carbenoid. It is not presently possible to distinguish whether the reactions are of the **MT-2$_{sync}$** or **MT-2$_{async}$** type or whether the processes are of a **MμS** or **SMμ** nature. The authors favor **MT-2$_{async}$**, **SMμ** processes with *trans* elimination of N_2 and catalyst. Such a phenomenon would be favored by the presence of bulky catalysts and is consistent with the major role of the catalyst being a Lewis acid.

EXPERIMENTAL

The major portion of the experimental is included in the following paper.[17] The diazoacetic ester was prepared by the method of Womach and Nelson.[18] Decompositions were conducted in a directly parallel fashion for both diazo compounds.[17] The iodo-trimethylphosphite copper(I) catalyst systems were prepared as previously described.[14]

Bis *acetylacetonato copper* (II). Cupric chloride dihydrate (85 g, 0·5 moles) was dissolved in 750 ml water. 2,4-Pentanedione (100 ml) was added with vigorous stirring. The soln turned deep blue and the blue copper(II) bis acetylacetonate began to rise to the surface. The mixture was stirred overnight. The dark blue crystals were filtered off and air dried. Recrystallization from chloroform gave mats of blue crystals, m.p. 238–9° (lit. 236° dec)[19,20] yield 20·7 g, 24·4%.

Bis (2,2,6,6 - *Tetramethylheptane* - 3,5 - *dionato*) *copper*(II). 2,2,6,6 - Tetramethylheptane - 3,5 - dione (9·2 g, 0·05 moles) was dissolved in 50 ml MeOH. Cupric acetate monohydrate (12 g, 0·06 moles) was dissolved in 100 ml boiling water and added and the product was filtered off (Buchner funnel) and air dried. Recrystallization from abs EtOH yielded purple crystals, m.p. 191·5–193·5° (lit. 192–3°C)[21], yield of recrystallized material was 7·71 g, 72%.

Catalyzed decomposition of ethyl diazoacetate in cyclohexene. Clean 100 ml round bottom flasks were prepared and assembled in the usual manner. A flask was charged with 25 ml cyclohexene, a variable amount of $Cu(AcAc)_2$ catalyst, and heated under reflux.

A soln of 2·28 g (0·02) ethyl diazoacetate in an additional 25 ml cyclohexene was added dropwise at the rate of 1 drop per 10 sec. After addition was complete, heating under reflux was continued overnight. The mixture was then concentrated *in vacuo* and analyzed by gas chromatography Components were identified by retention times.

REFERENCES

[1] For Paper XIII, see D. S. Wulfman, R. S. McDaniel, Jr. and B. W. Peace, *Tetrahedron* **32**, 1241 (1976).

[2a] Chercheur Associé au Centre National de la Récherche Scientifique (1974–1975); [b] Present address, UMR.

[3a] Taken in part from the Ph.D dissertation of B. W. Peace, University of Missouri-Rolla (1971); [b] Taken in part from the Ph.D dissertation of R. S. McDaniel, Jr., University of Missouri-Rolla (1974).

[4] The term "carbene dimer formation" is somewhat inexact but is to be preferred over "olefin formation" or "carbenoid dimer formation" because it most closely describes the nature of the product even though it does not arise by dimerization of the carbene. The fact that the process often occurs in the presence of olefins, makes the use of the word olefin more confusing than enlightening. We shall designate the reaction as being DF processes with no mention of the terms carbene or carbenoid.

[5] D. Bethell, *Advances in Physical Organic Chemistry*, (Edited by V. Gold). Academic Press, New York (1969).

[6] H. Werner and J. H. Richards, *J. Am. Chem. Soc.* **90**, 4976 (1968); *T. Sato*, *Tetrahedron Letters* 835 (1968); V. K. Jones and A. J. Deutschman, Jr., *J. Org. Chem.* **30**, 3978 (1965); A. G. Vitenberg, I. A. D'yakonov and A. Zindel, *Zh. Obsh. Khim.* **2**, 1532 (1966); M. Takebayshi, T. Shingaki, N. Torimoto and M. Inagaki, *Kogyo Kagaku Zasshi* **69**, 970 (1966).

[7] J. Font, F. Serratosa and J. Valls, *J. Chem. Soc.* Chem. Commun. 721 (1970).

[8] The authors experienced considerable difficulty in making a meaningful search of the literature on the subject and it is clear that far more examples exist than were found.

[9] The subject of olefin disproportionation of metatheses has received considerable attention. Sone lead refs can be found in *Annual Reports* **70B**, 266 (1973); **69B**, 278 (1972); **68B**, 285 (1971) and **67B**, 316 (1970).

[10] For examples of mistaken assignments as trimers see V. Dave and E. W. Warnhoff, *Organic Reactions* Wiley, New York (1972) and H. Werner and J. H. Richards, *J. Am. Chem. Soc.* **90**, 4976 (1968); R. G. Salomon and J. K. Kochi, *Ibid.* **95**, 3300 (1973), report the all *cis* trimer and if correct this represents a unique instance.

[11] A. Darapsky, *Ber. Dtsch. Chem. Ges.* **43**, 1112 (1910); E. Buchner and C. von der Heide, *Ibid* **34**, 345 (1901); E. Buchner and H. Witter, *Ann.* **273**, 239 (1893); O. Silberrad and C. S. Roy, *J. Chem. Soc.* **89**, 179 (1906); E. Buchner and H. Witter, *Ann.* **284**, 219 (1894); A. D. Forbes and J. Wood, *J. Chem. Soc.* (B) 1971, 646; and A. Darapsky, *Ber. Dtsch. Chem. Ges.* **43**, 1124 (1975).

[12] D. S. Wulfman, *Tetrahedron* **32**, 1231 (1976).

[13] B. W. Peace and D. S. Wulfman, *Synthesis* **137** (1973); *Tetrahedron Letters* 3799 (1971).

[14] D. S. Wulfman, N. V. Thinh, R. S. McDaniel, Jr., B. W. Peace, C. W. Heitsch and M. Tom Jones, *J. Chem. Soc.* Dalton Trans. 522 (1975).

[15] P. E. Krieger and J. A. Landgrebe, *9th Midwest Regional Meeting, Amer. Chem. Soc.* Paper 324, Lawrence, Kansas (1973).

[16] D. S. Wulfman, R. S. McDaniel, Jr. and B. W. Peace, *Tetrahedron* **32**, 1241 (1976).

[17] D. S. Wulfman, B. G. McGibboney, E. K. Steffen, N. V. Thinh, R. S. McDaniel, Jr. and B. W. Peace, *Tetrahedron* **32**, 1257 (1976).

[18] E. B. Womack and A. B. Nelson, *Org. Syn.* **24**, 56 (1944).

[19] F. C. Carman, M. S. Thesis, University of Missouri-Rolla (1969).

[20] B. Ciocca, *Gazz. Chim. Ital.* **67**, 346 (1937).

[21] E. H. Man, F. W. Swamer and C. R. Hauser, *J Am. Chem. Soc.* **73**, 901 (1951).