Catalyst–Product Dependency in the Transition Metal Catalyzed Decomposition of Ethyl 3-Diazo-2-oxopropionate. An Unusual Wolff Rearrangement

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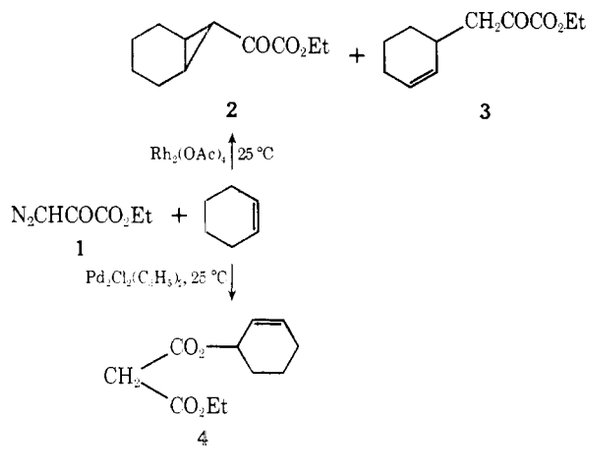
Competitive cyclopropanation, allylic insertion, and Wolff rearrangement have been observed in the catalytic decomposition of ethyl 3-diazo-2-oxopropionate in the presence of cyclohexene. The course of the decomposition could be controlled by use of transition-metal catalysts: highly selective formation of the norcaryl derivative **2** or the malonate **4** could be achieved by appropriate choice of catalyst. The formation of **4** has been interpreted by the concurrent metal-catalyzed oxidation of cyclohexene.

Recently attention has been focused on the influence of transition metal complexes on the selectivity of typical carbenoid reactions. Highly efficient specific catalysis has been observed in cyclopropanation of olefins,[1] in insertion into polar bonds,[2] and in oxazole formation from ketocarbenoids with nitriles.[3]

In a recent publication[4] we reported a well-defined catalyst–product dependency observed in the decomposition of ethyl 2-allyl-4-diazoacetoacetate, where the alternative formation of a bicyclohexanone or a furan-3(2*H*)-one system could be selectively controlled.

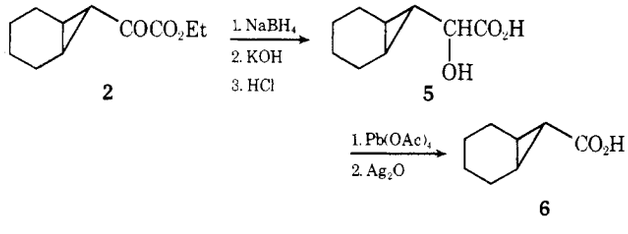
Another example of product control, dependent of the catalyst, is described here (Scheme I). We observed that the

Scheme I



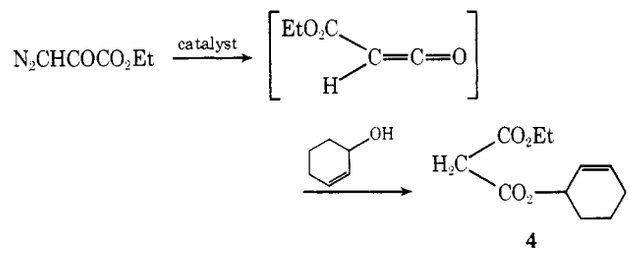
$Rh_2(OAc)_4$ induced decomposition of ethyl 3-diazo-2-oxopropionate (**1**) gave ethyl *exo*-7-norcarylglyoxylate (**2**) as major product, together with small amounts of **3**, formed by insertion into the allylic C–H bond. In contrast, decomposition with $Pd_2Cl_2(C_3H_5)_2$ led to the selective formation of ethyl cyclohex-2-enylmalonate (**4**) in high yield. Other metal complexes, previously used as effective catalysts in the decomposition of α-diazocarbonyl compounds, have also been applied and found to be nonselective (see Table I).

The exo configuration of compound **2** was proved by the sequence of reactions leading to the known *exo*-bicyclo[4.1.0]-heptane-7-carboxylic acid (**6**):



Copper, copper salts, and copper complexes are known to catalyze both the addition and insertion reactions of carbonyl carbenes with olefins.[5,6] The usefulness of $Pd(OAc)_2$ and the π-allylic $PdCl_2$ complex in cyclopropanation of olefins has also been demonstrated.[1a,b,7] On the other hand, Wolff rearrangement is known to be preferentially induced by silver (ion) catalysts, but supressed by copper salts.[5b,8] A specific keto carbene stabilization by complex formation has been also demonstrated for a palladium catalyst.[9]

In view of these facts, we can conclude that the formation of compounds **2** and **3** from the diazo ketone **1** and cyclohexene is not unexpected. In contrast, this is not the case with compound **4**. The formation of **4** may be rationalized by a simultaneous Wolff rearrangement of the diazo ketone and oxidation of the cyclohexene to cyclohex-2-en-1-ol followed by addition of the alcohol to the ketene:



Control reactions with cyclohexene and catalytic amounts of $Rh_2(OAc)_4$ or π-allylic $PdCl_2$ complex only, but without the diazo ketone **1**, confirmed the formation of cyclohex-2-en-1-ol, cyclohex-2-en-1-one (identification with GC), and some other unidentified oxidation products. The process was actually not hampered by the addition of the diazo ketone, since the same compounds were found in the low-boiling fractions of the crude products from the various decomposition reactions (see Experimental Section). Though the oxidation occurred in a very low overall yield (Rh was found to be somewhat more effective), the total amount of the formed cyclohex-2-en-1-ol appeared to be nearly equimolar to the added diazo compound. Consequently, in the presence of both catalysts, the malonate **4** could be a potential reaction product, provided that a ketenic precursor was formed by rearrangement of **1**. The complete absence of ester **4** in the reactions catalyzed by $Rh_2(OAc)_4$ but not by the π-allylic $PdCl_2$ complex clearly suggests, therefore, that the catalytic activity of the two complexes toward the Wolff rearrangement should be rather different.

For comparison, some of the decompositions were repeated under a static nitrogen atmosphere. In these experiments the Pd complex catalyzed formation of compound **4** was strongly suppressed indeed, thus indicating that oxidation to cyclohex-2-en-1-ol occurred to a much less extent.[10] On the other

Table I. Catalytic Decomposition of 1 in Cyclohexene

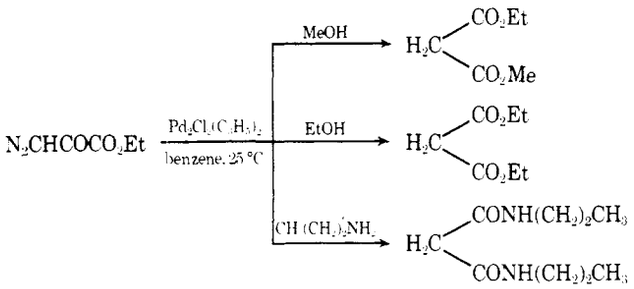
	Temp, °C	Time, h	Products, %[a,b] 2	3	4
$Pd_2Cl_2(C_3H_5)_2$	RT	4			79 (30)
Ag_2O	85	12			71
$Pd(C_6H_5COCHCOCH_3)_2$	85	12	51 (53)	22 (21)	5 (–)
$Cu(C_6H_5COCHCOCH_3)_2$	85	12	53	16	8
$CuCl{\cdot}P(OCH_3)_3$	85	12	48 (50)	18 (16)	23 (10)
$CuSO_4$	85	4	60	12	20
$Rh_2(OCOCH_3)_4$	RT	4	76 (76)	11 (12)	

[a] Yields are based on the diazo ketone 1. [b] The numbers in parentheses refer to yields obtained under N_2 atmosphere.

hand, the yields were found unchanged for the Rh-catalyzed cyclopropanation and allylic insertion reactions, where cyclohex-2-en-1-ol is not required as a product precursor. We believe, therefore, that decomposition of 1 is selectively controlled by the catalyst only, but is independent of the secondary process of olefin oxidation.

The π-allylic $PdCl_2$ complex induced rearrangement of diazo ketone 1 was further proved by trapping the ketene with methanol, ethanol, and *n*-propylamine in the absence of cyclohexene both under air and N_2 atmosphere (Scheme II).

Scheme II



Our results, as well as those of others, clearly support the accepted view, that decomposition of diazo carbonyl compounds is coordination controlled and thus the electronic and/or steric demands of the highly reactive metal complexed carbene should be product determining. At present, however, we have no explanation for the nature of the discriminative factors, operative in the coordination process, either to produce an apparently "free" carbene, prone to rearrange, or to develop a metal–carbene complex with an entirely reverse but high selectivity of catalyzing olefin cyclopropanation. These two extremes were observed by using the π-allylic $PdCl_2$ dimer and $Rh_2(OAc)_4$, respectively. All other catalysts used in this work effected nonselective decompositions, by producing intermediate carbenoids of some "dual nature". The almost identical product distribution obtained with $Pd(bzac)_2$ and $Cu(bzac)_2$ is especially important and suggests a possible dominating role of the ligands on the course of the decomposition. The use of the strongly coordinating ligand (bzac) seems to impose the same steric and, in part, electronic requirements on both of these catalysts. It is very likely, therefore, that the highly active, transient carbene–metal complexes in both cases will be of similar nature, thus leading to a similar product distribution, as observed. To our best knowledge this is the first example of a transition metal complex catalyzed Wolff rearrangement and the first reported case when the rearrangement involves the shift of a carbethoxy group, featuring the migration of a relatively electron-poor carbonyl carbon atom.

Further investigations will be necessary to determine a possible decisive influence of the α-keto ester moiety, located adjacent to the diazo group, on the course of the rearrangements. Preliminary experiments showed, that in the π-allylic $PdCl_2$ complex catalyzed decomposition of simple diazo ketones, as diazoacetophenone and diazoacetone, rearrangement occurred to an extent of 10–20% only.

Experimental Section[12]

Ethyl 3-Diazo-2-oxopropionate (1). This compound was prepared as previously described:[13] mp 72–74 °C; IR ($CHCl_3$) 2110, 1725, 1640 cm^{-1}; NMR δ 1.38 (t, 3 H, $-CO_2CH_2CH_3$) 4.36 (q, 2 H, $-CO_2CH_2CH_3$), 6.23 ppm (s, 1 H, $-CHN_2$).

Decomposition of the Diazo Ketone 1 in Cyclohexene on a Preparative Scale. A. With $(CH_3O)_3P{\cdot}CuCl$. A solution of diazo ketone 1 (2.84 g, 20 mmol) in freshly distilled cyclohexene (150 mL) was added dropwise to a magnetically stirred solution of $(CH_3O)_3P{\cdot}CuCl$ (40 mg, 0.2 mmol) in cyclohexene (150 mL) at 85 °C. After the addition was completed, stirring was continued overnight at the same temperature. Complete decomposition of the diazo ketone was shown by the disappearance of the IR band at 2110 cm^{-1}. The solution was filtered, and excess of cyclohexene was removed by distillation at atmospheric pressure. The oily residue (ca. 6.4 g) was then distilled in vacuo and fractions boiling at 30–70 °C (0.1 mm) and at 70–95 °C (0.1 mm) were collected. Qualitative GC analysis of the low-boiling fraction showed the presence of cyclohexene, cyclohex-2-en-1-ol, cyclohex-2-en-1-one, and another unidentified compound. By using dry column chromatography [silical gel (400 g) and hexane–benzene (1:4) as eluent] the higher boiling fraction was separated to three components: compound 3 was eluted first (0.6 g, 15.3%) followed by the norcaryl derivative 2 (1.66 g, 42.3%), and then by the malonate 4 (0.74 g, 17.5%). Analytical samples were obtained by GC on a 6 ft × 0.25 in. column of 3% XE-60 on 100–120 mesh Gas-Chrom Q at 140 °C (helium flow rate 80 mL min^{-1}).

Ethyl cyclohex-2-enylpyruvate (3) was a liquid: bp 70 °C (0.1 mm); IR ($CHCl_3$) 1735 cm^{-1}; NMR δ 1.10–2.20 (t overlapped by m, 10 H, $-CO_2CH_2CH_3$ and ring protons), 2.76 (m, 2 H, $-CH_2CO-$), 4.30 (q, $-CO_2CH_2CH_3$), 5.66 ppm (m, 2 H, $-CH{=}CH-$).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.60; H, 8.34.

Ethyl *exo*-7-norcarylglyoxylate (2) was a liquid: bp 80–81 °C (0.1 mm); IR ($CHCl_3$) 1700, 1725 cm^{-1}; NMR δ 1.10–2.23 (m overlapped by a t, 13 H, $-CO_2CH_2CH_3$ and ring protons), 2.58 (m, 1 H, $-CHCO-$), 4.28 ppm (q, 2 H, $-CO_2CH_2CH_3$).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.39; H, 8.16.

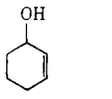
Ethyl cyclohex-2-enylmalonate (4) was a liquid: bp 73–74 °C (0.1 mm); IR ($CHCl_3$) 1720, 1740 cm^{-1}; NMR (CCl_4) δ 1.28 (t, 3 H, $-CO_2CH_2CH_3$), 1.46–2.26 (m, 6 H, ring methylenes), 3.23 (s, 2 H $-COCH_2CO-$), 4.16 (q, 2 H, $-CO_2CH_2CH_3$), 5.24 (m, 1 H, $-CO_2CH-$), 5.53–6.13 ppm (m, 2 H, $-CH{=}CH-$).

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found; C, 62.51; H, 7.71.

B. With Bis(chloro-π-allylpalladium). The same procedure as described under A was employed by using bis(chloro-π-allylpalladium) (72 mg, 0.2 mmol) as catalyst, with the exception that decomposition occurred at room temperature instead of at 85 °C. Workup was similar to that described under A. On distilling the crude product, after the low-boiling forerun, a major fraction of bp 73–76 °C (0.1 mm) was obtained and identified as the malonate 4 (3.3 g, 78%, over 95% purity by GC).

C. With $Rh_2(OAc)_4$. The procedure described under A was repeated by using $Rh_2(OAc)_4$ (88 mg, 0.2 mmol). The solution of the diazo ketone was added at room temperature and an adiitional stirring period of 2 h was necessary for complete decomposition. The workup,

Table II. Catalytic Oxidation of Cyclohexene to Cyclohex-2-en-1-ol and Cyclohex-2-en-1-one (Yields in mmol)

				
	Air	N_2	Air	N_2
$Pd_2Cl_2(C_3H_5)_2$	4.2[a]	2.0	2.3	1.1
$Rh_2(OAc)_4$	11.5	5.5	6.0	3.0

[a] This quantity, though representing only ca. 0.3% yield of oxidation, is nearly equimolar to the diazo ketone (5.0 mmol) used in the decomposition reactions. This explains the high-yield formation (79%) of compound **4** (see Table I).

similar to that described under A, gave the low-boiling oxidation products, followed by an oily mixture, bp 70–90 °C (0.1 mm) (3.6 g), which was purified by dry-column chromatography on silica gel (360 g, 70–200 mesh, activity grade II). Hexane–benzene mixture (1:4) eluted compound **3** (0.5 g, 10.2%), followed by the norcaryl glyoxylate **2** (2.75 g, 70.0%). A few intermediate fractions containing the mixture of compounds **2** and **3** were obtained as well.

Decomposition of the Diazo Ketone 1 in Cyclohexene with Various Catalysts. Product Distribution Study. The solution of the diazo ketone **1** (0.71 g, 5.0 mmol) in dry cyclohexene (60 mL) was added dropwise to a magnetically stirred suspension or solution of the various catalysts (5×10^{-2} mmol)[14] in dry cyclohexene (60 mL) at room temperature or at 85 °C in the presence of air or under static N_2 atmosphere (see Table I). The mixture was then stirred at the same temperature until complete decomposition of the diazo ketone was evidenced by the disappearance of the IR band at 2110 cm^{-1}. After filtration, the solvent was evaporated and the residue was weighed and analyzed by GC on 6 ft × 0.25 in. column of 3% XE-60 on 100–120 mesh Gas-Chrom Q at 140 °C. Mixed injections with authentic samples were used to identify the compounds **2, 3,** and **4.** Their yields calculated from the integration of the corresponding peaks are summarized in Table I.

Cyclohexene Oxidation Induced by $Rh_2(OAc)_4$ and $Pd_2Cl_2(C_3H_5)_2$. The solution of the catalyst (5×10^{-2} mmol) in dry cyclohexene (120 mL, percolated through alumina column) was stirred at room temperature under air or a static nitrogen atmosphere for 4 h. After filtration, the solvent was carefully evaporated and the residue was weighed and analyzed by GC on a 6 ft × 0.25 in. column of 3% XE on 100–120 mesh Gas-Chrom Q at 60 °C. Mixed injections with authentic samples were used to identify the two major peaks as corresponding to cyclohex-2-en-1-ol and cyclohex-2-en-1-one (see Table II).

Decomposition of the Diazo Ketone 1 with Bis(chloro-π-allylpalladium) in the Presence of Nucleophiles. A. A solution of the diazo ketone **1** (0.7 g, 5.0 mmol) in dry benzene (75 mL) was added dropwise during ca. 1.5 h to a magnetically stirred solution of the catalyst (18 mg, 0.05 mmol) in methanol (0.2 mL) and dry benzene (75 mL) at room temperature. Stirring was then continued for another 2 h for complete decomposition of the diazo ketone. After filtration, the solvent was evaporated and the oily residue (0.7 g) purified by high vacuum bulb to bulb distillation, to give ethyl methylmalonate (0.55 g, 76%) identical in spectral properties and GC retention time with an authentic sample.

B. The above procedure was repeated with ethanol (0.3 mL). The product (0.66 g, 83%) was identified as diethyl malonate.

C. The procedure described above was applied with *n*-propylamine (0.5 mL). The product was purified by column chromatography on alumina (70 g) to give *N,N'*-di-*n*-propylmalonamide (0.87 g, 89%), mp 141 °C (lit.[15] mp 140 °C).

The same results were obtained when the reactions described under A, B, and C were repeated under N_2 atmosphere.

Ethyl Cyclohex-2-enylmalonate (4). Cyclohex-2-en-1-ol (0.21 g, 2.2 mmol) in dry ether (25 mL) was added dropwise to a magnetically stirred solution of ethylmalonyl chloride (0.34 g, 2.3 mmol) and a drop of pyridine in dry ether (25 mL) at room temperature. After the addition was completed, the mixture was heated under reflux for 30 min. The cooled solution was then washed with saturated $NaHCO_3$ solution, the organic layer dried (Na_2SO_4), and the solvent removed. High-temperature distillation of the oily residue (0.5 g) gave 0.4 g (90%) of diester, bp 73–75 °C (0.1 mm). Spectral data were identical with those of compound **4** isolated from the decomposition of **1** in cyclohexene (see above).

***exo*-7-Norcarylethanediol and *exo*-7-Norcarylglycolic Acid (5).** An ice-cold magnetically stirred solution of the keto ester **2** (7.8 g, 0.04 mol) in absolute ethanol (150 mL) was treated portionwise with $NaBH_4$ (1.51 g, 0.04 mol). After 0.5 h, the ethanol was removed under vacuum, saturated NaCl solution was added, and the mixture was extracted several times with chloroform. The combined chloroform extracts were washed with H_2O until neutral pH and dried (Na_2SO_4). After removal of the solvent, the residue (6.9 g) was dissolved in ethanol (100 mL), a solution of KOH (2.3 g) in ethanol (100 mL) was added, and the mixture was stirred magnetically at room temperature overnight. After removal of the ethanol, saturated NaCl solution (100 mL) was added and the mixture extracted with chloroform (2 × 75 mL). From the dried (Na_2SO_4) chloroform extract the glycol **7** was obtained as a thick oil, which solidified on standing (1.4 g, 24%): mp 52–54 °C (from hexane–pentane, 3:2); IR ($CHCl_3$) 3400–3600 cm^{-1}; NMR δ 0.36–1.00 (m, 3 H, cyclopropyl), 1.00–2.30 (m, 8 H, cyclohexane CH_2), 2.80–4.00 ppm (m, 3 H, -CHOH-CH_2OH).

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.44; H, 10.22.

The aqueous alkaline phase was acidified (pH 1–2) with 10% aqueous HCl solution and extracted with chloroform. After the usual workup, 4.4 g (65%) of the hydroxy acid **5** was isolated, mp 116–117 °C. Recrystallization from cyclohexane gave the pure acid: mp 119–121 °C; IR ($CHCl_3$) 1725, 2500–3000 cm^{-1}; NMR δ 0.50–2.33 (m, 11 H), 3.80 (d, 1 H, -CHOH), 5.53 ppm (br s, 2 H, -CHOH and -COOH).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.62; H, 8.55.

***exo*-Bicyclo[4.1.0]heptane-7-carboxylic Acid (6).** To a magnetically stirred solution of the hydroxy acid **5** (0.42 g, 2.5 mmol) in dry benzene (30 mL), freshly recrystallized $Pb(OAc)_4$ (1.27 g, 2.8 mmol) was added in portions at room temperature. After the addition was completed, stirring was continued for another 15 min. The solution was then filtered, washed with water, and dried. Evaporation of the solvent gave crude 7-formylbicyclo[4.1.0]heptane (0.3 g): IR ($CHCl_3$) 1730, 2720 cm^{-1}; NMR δ 1.0–2.2 (m, 11 H), 9.1 ppm (d, 1 H, -CHO). The crude aldehyde was dissolved in ethanol (2 mL), and a solution of $AgNO_3$ (1.8 g) in H_2O (30 mL) was added, followed by dropwise addition of NaOH (0.6 g) in H_2O (6 mL). The mixture was stirred at room temperature for 30 min, then filtered and acidified with 10% HCl solution. Extraction with ether, drying on Na_2SO_4, and evaporation of the solvent gave the acid **6** (0.31 g, 88%): mp 96–97 °C (lit.[16] mp 97–99 °C); IR ($CHCl_3$) 1690, 2500–3000 cm^{-1}; NMR δ 1.08–2.17 (m, 11 H), 12.1 ppm (s, 1 H, -COOH).

Registry No.—**1,** 14214-10-9; **2,** 61558-26-7; **3,** 61558-27-8; **4,** 61558-28-9; **5,** 61558-29-0; **6,** 21448-77-1; **7,** 61558-30-3; cyclohexene, 110-83-8; cyclohex-2-en-1-ol, 822-67-3; ethylmalonyl chloride, 36239-09-5.

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(10) This result is not completely understood, since under N_2 atmosphere complete elimination of oxidation was expected. We can suggest a possible explanation for the partial oxidation process by considering that various transition metal complexes have been proved to catalyze olefin-autoxidation reactions by decomposing small amounts of hydroperoxides, always present in unsaturated hydrocarbons.[11] The cyclohexene used gave a weak positive test for peroxides, even after pretreatment with alumina. Presumably, the residual peroxides and oxygen in the different batches (120 mL, 1.15 mol each) were in a concentration high enough to be considered as potential reagents for the observed oxidation. In support, we found, that the Pd-catalyzed decomposition, when only a small excess of the cyclo-

hexene (2 mL, 19 mmol) in benzene solution was used, led to a complex mixture of products, mostly polymeric, but compounds **2**, **3** and **4** were absent. A more detailed, quantitative investigation of the oxidation process was beyond our original research interest.

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(12) Melting points were taken in capillaries and are uncorrected. The IR spectra were determined on a Perkin-Elmer Infracord spectrophotometer. NMR spectra were recorded on a Varian T-60 or on a Varian A-60 spectrometer in $CDCl_3$ solution using Me_4Si as internal standard. GC analyses were done on a Varian Aerograph Model 90-P gas chromatograph.

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Isolation and Reactions of α-Lithio *N,N*-Dimethylacetamide

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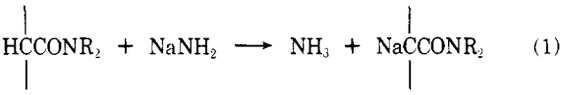
α-Lithio *N,N*-dimethylacetamide (**1**) was obtained as a white solid by reaction of *N,N*-dimethylacetamide with lithium diisopropylamide in pentane. From ^1H NMR evidence, a lithium–oxygen bonded structure is proposed. THF solutions of **1** could be generated at 0 °C and were stable for several days at room temperature. Reactions of **1** with organic halides, aldehydes, ketones, and epoxides are described.

Although metalated derivatives of amides possessing α-aryl or other carbanion-stabilizing groups were known much earlier,[2] the first syntheses of α-metalated derivatives of simple *N,N*-dialkylamides were reported in 1966 by Gassman[3] and by Needles[4] using sodamide as the base in liquid ammonia[3] or benzene[4] (eq 1). Since that time, lithiated amides have



$$\text{HCCONR}_2 + \text{NaNH}_2 \longrightarrow \text{NH}_3 + \text{NaCCONR}_2 \qquad (1)$$

been made using lithiated 1,3,5-trithiane as base,[5] or, more efficiently, lithium diethylamide in hexamethylphosphoramide[6] or lithium diisopropylamide in tetrahydrofuran (THF).[7-9]

We describe here our own observations on the preparation of lithiated *N,N*-dimethylacetamide and its reactions with a variety of electrophiles.

Results and Discussion

Stability and Isolation of Lithio *N,N*-Dimethylacetamide. Solutions of α-lithio *N,N*-dimethylacetamide (**1**) were prepared by dropwise addition of *N,N*-dimethylacetamide (**2**) to THF solutions of lithium diisopropylamide at dry ice temperature. Quenching the solutions with glacial acetic acid gave 95–100% recovery of the amide (eq 2). Solutions of **1** allowed to reach room temperature remained homogeneous and colorless. Quenching returned 90–95% of **2** after 19 h at room temperature, and 75–80% after 3 days. Small amounts (5–10%) of the condensation product, *N,N*-dimethylacetoacetamide, were detected in the quenched mixtures after 1 day. Identical results were obtained by preparing **1** at 0 °C in THF rather than at −78 °C.

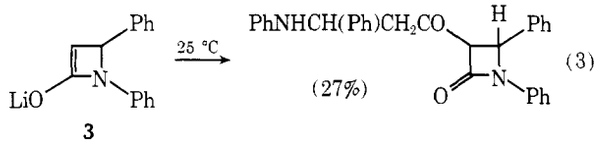
$$\underset{\mathbf{2}}{\text{CH}_3\text{CON(CH}_3)_2} + \text{LiN[CH(CH}_3)_2]_2 \xrightarrow[-78\ ^\circ\text{C}]{\text{THF}} \underset{\mathbf{1}}{\text{LiCH}_2\text{CON(CH}_3)_2} + \text{HN[CH(CH}_3)_2]_2$$

$$\xrightarrow[-78\ ^\circ\text{C}]{\text{HOAc}} \text{LiOAc} + \text{CH}_3\text{CON(CH}_3)_2 \qquad (2)$$

(95–100%, GLC)

Addition of **2** to solutions of lithium diisopropylamide in pentane at 0 °C resulted in the immediate formation of a white precipitate. Removal of solvent and amine under reduced pressure gave **1** as a white solid in quantitative yield. Quenching weighed samples of the solid with glacial acetic acid returned **2** in 90% yield. Exposure to air for several minutes turned the solid black; however, samples of the solid were stored in sealed bottles for several weeks with no evidence of change (as judged by appearance and by recovery of **2** on quenching). The ^1H NMR spectrum of the solid (pyridine solution) shows two partially resolved doublets (δ 3.15, 1 H, 2.93, 1 H) and a sharp singlet (δ 2.63, 6 H).

Solutions of α-lithio *N,N*-dimethylacetamide have been obtained previously,[5-7] but there are no prior reports of its stability or of attempts to isolate the pure material. The lithium enolate of a β-lactam, **3**, was reported to be reasonably



$$\xrightarrow[25\ ^\circ\text{C}]{} \text{PhNHCH(Ph)CH}_2\text{CO} \quad (27\%) \qquad (3)$$

3

stable at −78 °C, but condensation occurred (27%) on warming a THF solution to room temperature for 20 min.[8] From the method of preparation and reaction with organic halides[4] (several hours in refluxing benzene, 5–60% yields of alkylation products) it may be deduced that sodio *N,N*-dimethylacetamide (**4**, eq 4) is much more stable than this.

$$\text{CH}_3\text{CON(CH}_3)_2 \xrightarrow[\text{C}_6\text{H}_6,\ 65\ ^\circ\text{C}]{\text{NaNH}_2} \underset{\mathbf{4}}{\text{NaCH}_2\text{CON(CH}_3)_2} \xrightarrow[65\ ^\circ\text{C}]{\text{RX}} \text{RCH}_2\text{CON(CH}_3)_2 \qquad (4)$$

Our results indicate that **1** is sufficiently stable that its solutions may be generated at 0 °C rather than the usual −78 °C. Its stability is especially high when compared to analogous lithium ester enolates. For example, solutions of lithio *tert*-butyl acetate (**5**)[10] have a half-life of less than 2 h at room temperature (eq 5).[11]

$$\underset{\mathbf{5}}{\text{LiCH}_2\text{CO}_2\text{C(CH}_3)_3} \xrightarrow[25\ ^\circ\text{C}]{\text{THF}} \text{LiOC(CH}_3)_3 + [\text{CH}_3\text{COCHCO}_2\text{C(CH}_3)_3]\text{Li} \qquad (5)$$