# Novel Synthesis of *trans*-Hydroindenones by Thermal Reaction of α,ω-Bis(diazo)diketones

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Thermal reaction of α,ω-bis(diazo)diketones gives α,β-unsaturated cycloalkenones including unsubstituted *trans*-hydroindenones, which were difficult to access by the conventional synthetic reactions.

The reactions of α-diazocarbonyl compounds have been the subject of intensive research in synthetic organic chemistry.[1] The utilization of metal catalysts in the decomposition of α-diazocarbonyl compounds has met with great success in cyclopropanation,[2] C–H or O–H insertion,[3] dipolar cycloaddition,[4] ylide formation[5] and other reactions[6] involving their metal carbenoids. On the other hand, although the thermal reaction of α-diazocarbonyl compounds to induce Wolff rearrangement has been frequently employed in one-carbon homologation of carboxylic acid and ring contraction,[7] it has been relatively unused in synthesis.[8] We, herein, report that the thermal activation of α,ω-bis(diazo)diketones provides novel cyclopentenone as well as cyclohexenone cyclization reactions.

The thermal reactions of α,ω-bis(diazo)diketones have been investigated in protic media to produce diacid derivatives resulting from the initial Wolff rearrangement of each diazoketone followed by nucleophilic attack of solvent or additive addition to the ketene formed.[9,10] In aprotic solvent, however, the thermal reaction of α,ω-bis(diazo)diketones was found to follow a completely different reaction course as shown in Scheme 1.
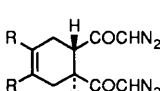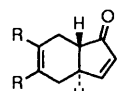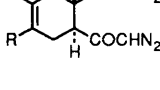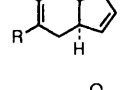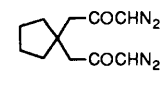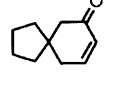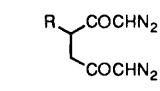
Thus, *trans*-bis(diazo)diketone **2** prepared from *trans*-cyclohexane-1,2-dicarboxylic acid chloride **1** with diazomethane was treated in refluxing toluene to produce a single compound **3**, the molecular formula of which was determined by high resolution mass spectra (HRMS) as $C_9H_{12}O$. The existence of α,β-unsaturated carbonyl functionality of the partial structure was suggested by ^{1}H NMR spectrum, in which two vinylic hydrogens were observed at δ 6.03 (dd, 1H, J 6.1, 2.4 Hz, 2-H) and 7.46 (br, 1H, J 6.1 Hz). This value was obtained by decoupling the signal at δ 2.36, 3-H). On the other hand, the thermal 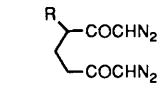reaction of the *cis*-bis(diazo)diketones **5** required a higher temperature (170 °C in toluene in a sealed tube) and produced a compound with the same molecular formula ($C_9H_{12}O$) in HRMS as **2** but a different ^{1}H NMR spectrum [δ 6.13 (dd, 1H, J 5.5, 1.8 Hz, 2-H) and 7.62 (dd, 1H, J 5.5, 2.8 Hz, 3-H) for two vinylic hydrogens], which was found to be identical to that of *cis*-hydroindenone **6**.[11] The structure of **3** was, thus, elucidated as the unprecedented

*trans*-hydroindenone as shown.† In the case of the product **10** obtained by the thermal reaction of **9**, its structure involving the *trans*-hydroindenone system was confirmed by single crystal X-ray analysis.

This novel thermal cyclization of α,ω-bis(diazo)diketones was found to be a general reaction to give cycloalkenone derivatives (Table 1). The most significant feature of this reaction was the production of unsubstituted *trans*-hydroindenones. Thus, upon thermolysis of *trans*-bis(diazo)diketones, **2, 7** and **9**, unprecedented *trans*-hydroindenones **3, 8** and **10** could be produced in good to excellent yields. Although *trans*-hydroindenones with angular methyl groups at the α position to the carbonyl group were protected from epimerization, the unsubstituted *trans*-hydroindenones were unstable under basic conditions. Since this thermal reaction could be carried out in completely neutral conditions, the stereochemsitry at α to the carbonyl groups in the starting bis(diazo)diketones was completely retained.

Since the thermal reaction of symmetrical bis(diazo)diketones afforded unsymmetrical enones (entry, 1, 2, 3), two isomeric products were anticipated to form from unsymmetrical bis(diazo)diketones (entry 4–7). Thus, thermolysis of **13** gave the γ- and α'-substituted cyclopentenones **14** and **15** in

**Table 1** Thermal reaction of α,ω-bis(diazo)diketones



| Entry | Bis(diazo)diketones | Product(s) | Yield (%)[c] |
|---|---|---|---|
| 1 | **7**[a]; R = H | | **8** 54[d] |
| 2 | **9**[a]; R = Me | | **10** 53 |
| 3 | **11**[b] | | **12** 68 |
| 4 | **13**[b]; R = decyl | **14** (32:68)[e] | **15** 81[g] |
| 5 | **16**[b]; R = Ph | **17** (47:53)[e] | **18** 82[g] |
| 6 | **19**[b]; R = decyl | **20** (28:72)[f] | **21** 45[g] |
| 7 | **22**[b]; R = Ph | **23** (38:62)[f] | **24** 44[g] |

All reactions were performed at 0.01 mol dm⁻³ concentration in toluene at either [a] refluxing or [b] 170 °C in a sealed tube. [c] Isolated yield otherwise noted. [d] ^{1}H NMR yield. The ratio of two isomers was determined by either [e] GLC or [f] ^{1}H NMR analysis. [g] Combined yield.

† The *trans* stereochemistry of **3** was supported by the small coupling constant observed between H-3 and H-4 in ^{1}H NMR spectrum of **3**, which was in good agreement with that of estimated from the dihedral angle (∠3-H-C-3-C-4-4-H : 84.4°) obtained from the conformational analysis of **3** using MNDO-PM3 calculation (MOPAC ver 5.01, J. J. P. Stewart).
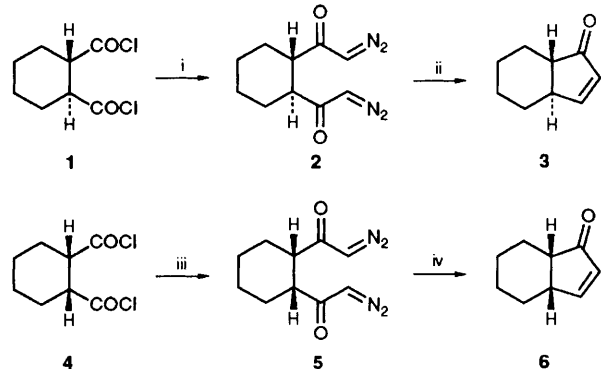


**Scheme 1** *Reagents and conditions*: i, $CH_2N_2$, diethyl ether, 0 °C, 48%; ii, toluene reflux, 92%; iii, LiC(N₂)SiMe₂Ph, diethyl ether, 0 °C, 27%; iv, toluene, 170 °C (in a sealed tube), 72%
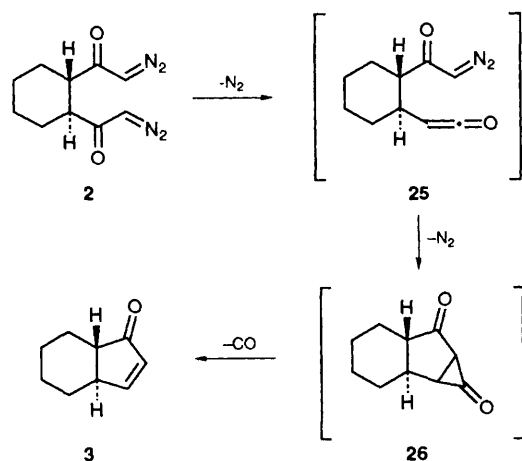
**Scheme 2**

81% yield in a ratio of 32:68. With the limited examples we have investigated the γ-substituted enones seemed to be the major products although selectivity was not high.

From the material balance in this reaction exclusion of two dinitrogens and one carbon monoxide was considered (Scheme 2). Taking into account Wolff rearrangement as the initial step, the produced diazoketene **25** would undergo subsequent decomposition to produce the possible intermediate, cyclopropanone **26**, from which thermal elimination of carbon monoxide has been well investigated.[12] Although the mechanism for the second step (*e.g.* **25** → **26**) was not clear, the intramolecular 1,3-dipolar cycloaddition reaction of α-diazoketones to the ketene[13] followed by elimination of $N_2$ is conceivable.‡

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‡ Another possibility involving the acylation of ketene with the second diazoketone followed by Favorskii type reaction of the produced α'-diazonium ketone enolate to reach the same cyclopropanone is also conceivable. See reference 12. One referee commented that this was a more probable mechanism than that involving 1,3-dipolar cycloaddition.

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