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FACILE SYNTHESES OF (Z)- AND (E)-2,5-DIMETHYL-3-STYRYLPYRAZINES, ISOLATED FROM THE ARGENTINE ANTS

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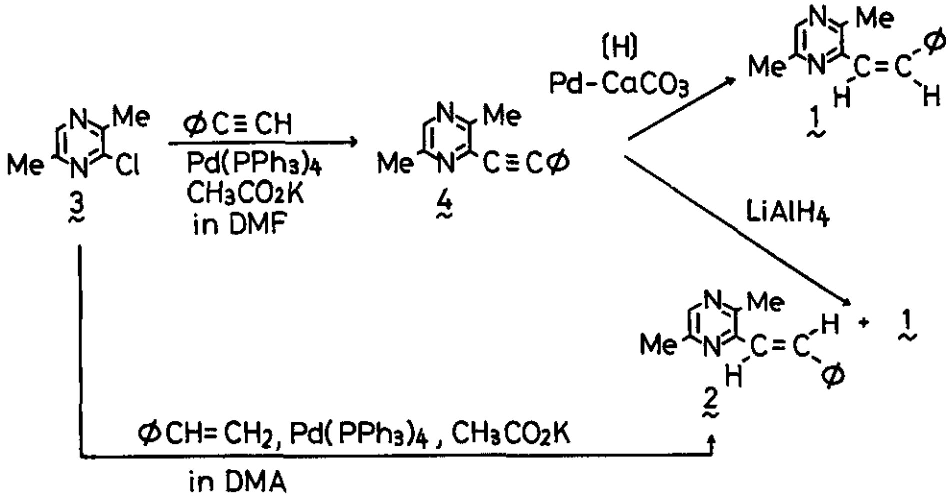
Abstract --- Syntheses of (Z)- and (E)-2,5-dimethyl-3-styrylpyrazines, isolated from *Iridomyrmex humilis*, were performed by replacing the chlorine atom of 3-chloro-2,5-dimethylpyrazine with C-substituents, utilizing tetrakis(triphenylphosphine)palladium as catalyst.

A number of trialkylpyrazines have been isolated from mandibular gland secretions of several species of ants.[1] Among these pyrazines, (Z)- and (E)-2,5-dimethyl-3-styrylpyrazines (**1** and **2**) are known as constituents of the Argentine ants, *Iridomyrmex humilis*.[2] The present paper describes briefly the syntheses of **1** and **2** by a cross-coupling reaction between 3-chloro-2,5-dimethylpyrazine[3] (**3**) and unsaturated compounds, such as phenylacetylene and styrene, in the presence of tetrakis(triphenylphosphine)palladium.[4]

Recently, we have reported the dechlorination of the chloropyrazines and their N-oxides,[5] and the introduction of the cyano group in the pyrazine ring,[6] using tetrakis(triphenylphosphine)palladium as catalyst. After that we have studied to explore an efficient utilization of this catalyst for the syntheses of the pyrazine derivatives and found that this catalyst was suitable for the coupling reaction of **3** with phenylacetylene and styrene. A mixture of **3** (1 mmol), the catalyst (0.05 mmol), potassium acetate (1.5 mmol) and phenylacetylene (1.5 mmol) in N,N-dimethylformamide (5 ml) was heated at 100 °C for 2 hr in argon stream to give 2,5-dimethyl-3-phenylethynylpyrazine (**4**) in 84% yield. In the case of the reaction with styrene, N,N-dimethylacetamide was used as solvent and the reaction mixture was refluxed for 15 hr to afford **2** in 95% yield. For the preparation of **1**, **4** was hydrogenated in a hexane solution over the Lindlar catalyst in quantitative yield.

The reduction of **4** was carried out also with lithium aluminum hydride under reflux in tetrahydrofuran[7] and the products were purified by chromatography on a silica gel to yield **1** (8%) and **2** (14%). The spectral data[8] of **1** and **2** were identical with those of the natural products.[2]



Although there are some reports[9, 10] on the cross-coupling reactions of halogenated aromatic N-heterocycles using palladium catalysts, the results obtained in this paper suggest that tetrakis(triphenylphosphine)palladium is also an effective catalyst for the coupling reaction of chloropyrazines with alkynes and alkenes. Further work is in progress on the introduction of C-substituents in the pyrazine ring.

REFERENCES AND NOTES

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8 **1**, colorless oil, bp 108-115°/3 torr (oil bath temp.). Mass: m/e 210 (M^+). PMR ($CDCl_3$) δ : 2.26 (3H, s), 2.46 (3H, s), 6.62 (1H, d, J = 11 Hz), 6.86 (1H, d, J = 11 Hz), 6.90-7.40 (5H, m), 8.21 (1H, s). UV (95% EtOH) nm ($\log \varepsilon$): 252 (3.83, shoulder), 279 (3.90), 315 (3.72, shoulder).

2, colorless oil, bp 117-122°/3 torr (oil bath temp.). Mass: m/e 210 (M^+). PMR ($CDCl_3$) δ : 2.54 (3H, s), 2.62 (3H, s), 7.20 (1H, d, J = 16 Hz), 7.30-7.48 (3H, m), 7.48-7.65 (2H, m), 7.82 (1H, d, J = 16 Hz), 8.16 (1H, s). UV (95% EtOH) nm ($\log \varepsilon$): 230 (4.00), 236 (3.97, shoulder), 275 (4.18), 333 (4.24).

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